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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,747	10/18/2005	Teruyuki Kobayashi	1204.45527X00	5938

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EXAMINER	
BHAT, NARAYAN KAMESHWAR	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,747	KOBAYASHI ET AL.	
	Examiner	Art Unit	
	NARAYAN K. BHAT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 21-26* is/are pending in the application.

4a) Of the above claim(s) *8-16 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 17, 19 and 21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 28, 2008 has been entered.

Status of the Claims

2. This action is in response to papers filed on April 28, 2008, wherein claims 1, 19, were amended and claim 20 was cancelled.

3. The previous rejections under 35 USC § 102 (b) and 103(a) are withdrawn in view of amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections.

4. Claims 1-19 and 21-26 are pending in this application.

5. Claims 1-7, 17, 19 and 21-26 are under examination.

Amendments to the Claims

6. Amendments to claims 1 and 19 have been reviewed and entered.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-5, 17, 19, 21, 22, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al (Nano Letters, 2002, 2, 863-867) in view of Obremski et al (USPGPUB NO. 2002/0001853 published Jan. 3, 2002) and further in view of Seong et al (Anal. Chem. 2000, 72, 1288-1293).

Regarding claim 1, Liu et al teaches a molecular detection method comprising visualizing and identifying chain molecule (Figs. 4A and 4G, pg. 865, column 2, paragraph 3) immobilized on a substrate in upright position (Fig. 1, pg. 865, column 1, paragraph 1) by probing with scanning probe microscope in solution (Abstract, Figs. 3A

and 4A, pg. 865, column 2, paragraph 2). Liu et al are silent about plastic substrate and visualizing and identifying an individual chain molecule.

Regarding claim 2, Liu et al teaches that chain molecule (i.e., single stranded DNA) is immobilized on the gold surface (Fig. 2C, pg. 864, column 1, and last paragraph) and is an uprightly disposed single stranded DNA molecule (i.e., stand up configuration, pg.865, column 1, paragraph 1).

Regarding claim 3, Liu et al teaches that the uprightly single strand molecule is a nucleic acid (Fig. 1, pg. 865, column 1, paragraph 1)

Regarding claim 4, Liu et al teaches that the chain molecule is in stand up position (Fig. 1, pg. 865, column 1, paragraph 1) and the binding of DNase I molecule to the uprightly disposed chain molecule thus comprises multi-strand molecule.

Regarding claim 5, Liu et al teaches that the multiple strand molecules are a complex of single strand DNA and protein DNaseI (pg. 865, column 2, paragraphs 2 and 3, pg. 866, column 1, paragraph 1).

Regarding claim 17, Liu et al teaches a production process for immobilizing the single stranded DNA, i.e., chain molecule on a substrate (Fig. 2, substrate – labeled as Au (III), pg. 864, column 1, paragraph 4) and further teaches that the immobilized single strand DNA is in uprightly disposed position (Fig. 1, pg. 865, column 1, paragraph 1).

Regarding claim 19, Liu et al teaches a molecular detection method comprising visualizing and identifying chain molecule (Figs. 4A and 4G, pg. 865, column 2, paragraph 3) immobilized on a substrate in upright position (Fig. 1, pg. 865, column 1, paragraph 1) by probing with scanning probe microscope in solution (Abstract, Figs. 3A

and 4A, pg. 865, column 2, paragraph 2), wherein the molecule immobilized on the substrate is a nucleic acid (Fig. 2, pg. 864, column 1, paragraph 3). Liu et al are silent about plastic substrate and visualizing and identifying an individual chain molecule.

Regarding claim 21, Liu et al teaches that the chain molecule is in stand up position (Fig. 1, pg. 865, column 1, paragraph 1) and the binding of DNase I molecule to the uprightly disposed chain molecule thus comprises multi-strand molecule.

Regarding claim 22, Liu et al teaches that the multiple strand molecules are a complex of single strand DNA and protein DNaseI (pg. 865, column 2, paragraphs 2 and 3, pg. 866, column 1, paragraph 1).

Regarding claim 25, Liu et al teaches a production process for immobilizing the single stranded DNA, i.e., chain molecule on a substrate (Fig. 2, substrate – labeled as Au (III), pg. 864, column 1, paragraph 4) and further teaches that the immobilized single strand DNA is in uprightly disposed position (Fig. 1, pg. 865, column 1, paragraph 1).

Regarding claim 26, Liu et al teaches the substrate is gold (Fig. 2, pg. 864, column 1, last paragraph), but is silent about plastic surface.

Regarding claims 1, 19 and 26, Liu et al are silent about plastic substrate. However, a plastic substrate for immobilizing chain molecules were known in the art at the time of the claimed invention was made as taught by Obremski et al who teaches an assay method comprising a plastic substrate (paragraph 0038) for immobilizing oligonucleotide probe (paragraph 0010). Obremski et al also teaches that plastic surface is optically transparent, has a higher refractive index than water, easy to configure to different dimensions and amenable for chemical coupling and is well suited

for AFM and evanescent wave excitation method molecular detection (paragraphs 0038 and 0071).

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the molecular detection method of Liu et al and include the method of immobilizing the nucleic acid on the plastic surface of Obremski et al with a reasonable expectation of success.

An artisan would have been motivated to modify the molecular detection method of Liu et al and include the method of immobilizing the nucleic acid on the plastic surface of Obremski et al with the expected benefit of having a plastic surface, that is optically transparent, has a higher refractive index than water, easy to configure to different dimensions and amenable for chemical coupling and is well suited for AFM and evanescent wave excitation molecular detection as taught by Obremski (paragraphs 0038 and 0071), thus expanding the utilities of molecular detection method of Liu et al.

Regarding claims 1 and 19, Liu et al teaches the visualizing and identifying about 26 molecules in an 80.5 nm2 area (Fig. 3E, lane a2, area indicated by an arrow, pg. 865, column 1, paragraph 2). Obremski et al also teaches an AFM scanning of immobilized avidin array and further teaches that avidin extends 200 nm vertically from the surface and binds to biotin (paragraph 0071). Liu et al and Obremski et al are silent about visualizing and identifying an individual chain molecule by scanning probe microscope in solution. However, visualizing and identifying an individual chain

molecule by scanning probe microscope in solution was known in the art at the time of the claimed invention was made as taught by Seong et al.

Seong et al teaches visualization and identification of RecA protein binding to the single stranded DNA by scanning the complex by AFM in solution (Abstract, pg. 1288, column 1, and paragraph 1). Seong et al also teaches visualization and identification of single chain molecule (i.e., target DNA, Abstract). Combined teachings of Liu et al, Obremski et al and Seong et al, thus would provide a method of visualizing and identifying a single strand DNA individual chain molecule uprightly immobilized on a plastic substrate by probing with an AFM scanning probe microscope in solution.

Seong et al also teaches that the AFM imaging allows to study small proteins binding to their individual target sequences under native conditions and for gene mapping on individual double stranded DNA for further enhancing the understanding of macromolecular interactions responsible for genetic and cellular regulation (pg. 1289, column 1, paragraphs 1 and 2).

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the molecular detection method of Liu et al and Obremski et al and include the method of visualizing and identifying individual chain molecule of Seong et al with a reasonable expectation of success.

An artisan would have been motivated to modify the molecular detection method of Liu et al and Obremski et al and include the method of visualizing and identifying individual chain molecule of Seong et al with the expected benefit of studying small proteins binding to their individual target sequences under native conditions and for

gene mapping on individual double stranded DNA for further enhancing the understanding of macromolecular interactions responsible for genetic and cellular regulation as taught by Seong et al (pg. 1289, column 1, paragraphs 1 and 2).

10. Claims 1-3, 6-7, 19, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al (USPN 7,033,476 filed Dec. 31, 2002) in view of Obremski et al (USPGPUB NO. 2002/0001853 published Jan. 3, 2002).

Regarding claims 1 and 19, Lee et al teaches a molecular detection method comprising visualizing and identifying single molecules by probing with scanning probe microscope in solution (Fig. 5, Scanning probe, # 78, column 5, lines 40-52). Lee et al further teaches that a nonogate is formed on the substrate (Fig. 4, Substrate # 40, nanogate # 42) and nucleic acid sample molecules are held at the gate by perpendicular electric field (Fig. 4, column 4, line 60, column 5, lines 53-58, column 8, lines 43-67), thus teaching single molecules are immobilized uprightly on the substrate. Lee et al are silent about plastic substrate.

Regarding claims 2 and 3, Lee et al teaches that single strand molecule is a protein (column 5, line 28).

Regarding claims 6, 7, 23 and 24, Lee et al teaches detecting and counting single molecule immobilized within the nanogate (column 8, lines 43-67) thus teaching number of detected molecules per unit area, thus giving the molecular localization information.

Lee et al are silent about plastic substrate. However, a plastic substrate for immobilizing chain molecules were known in the art at the time of the claimed invention was made as taught by Obremski et al who teaches an assay method comprising a plastic substrate (paragraph 0038) for immobilizing oligonucleotide probe (paragraph 0010). Obremski et al also teaches that plastic surface is optically transparent, has a higher refractive index than water, easy to configure to different dimensions and amenable for chemical coupling and is well suited for AFM and evanescent wave excitation method molecular detection (paragraphs 0038 and 0071).

It would have been prima facie obvious to one having the ordinary skill in the art at the time the invention was made to modify the molecular detection method of Lee et al and include the method of immobilizing the nucleic acid on the plastic surface of Obremski et al with a reasonable expectation of success.

An artisan would have been motivated to modify the molecular detection method of Lee et al and include the method of immobilizing the nucleic acid on the plastic surface of Obremski et al with the expected benefit of having a plastic surface, that is optically transparent, has a higher refractive index than water, easy to configure to different dimensions and amenable for chemical coupling and is well suited for AFM and evanescent wave excitation molecular detection as taught by Obremski (paragraphs 0038 and 0071), thus expanding the utilities of molecular detection method of Lee et al.

Response to remarks from the Applicants

Claim rejections under 35 U.S.C. § 102(b)

11. Applicant's arguments filed on March 26, 2008, regarding teachings of Henderson et al and Liu et al have been fully considered but are moot in view of the new grounds of rejection (Remarks pgs. 8-14).

Claim rejections under 35 U.S.C. § 103(a)

12. Applicant's arguments filed on March 26, 2008, regarding teachings of Henderson et al in view of Liu et al have been considered but are moot in view of the new grounds of rejection (Remarks pgs. 8-14). Applicant's arguments as relate to the teachings of Liu et al in this office action are addressed below.

Applicant argues that "Liu et al teaches visualizing and identifying the aggregate" (Remarks, pg. 14, paragraph 1). This argument is not persuasive because as discussed above, Liu et al teaches that the single stranded DNA immobilized on the surface are uprightly disposed single stranded DNA. Furthermore, Seong is relied upon for individual molecule analysis.

Conclusion

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Narayan K. Bhat whose telephone number is (571)-272-5540. The examiner can normally be reached on 8.30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla can be reached on (571)-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Narayan K. Bhat/

Examiner, Art Unit 1634

Narayan K. Bhat, Ph. D.

/BJ Forman/

Primary Examiner, Art Unit 1634